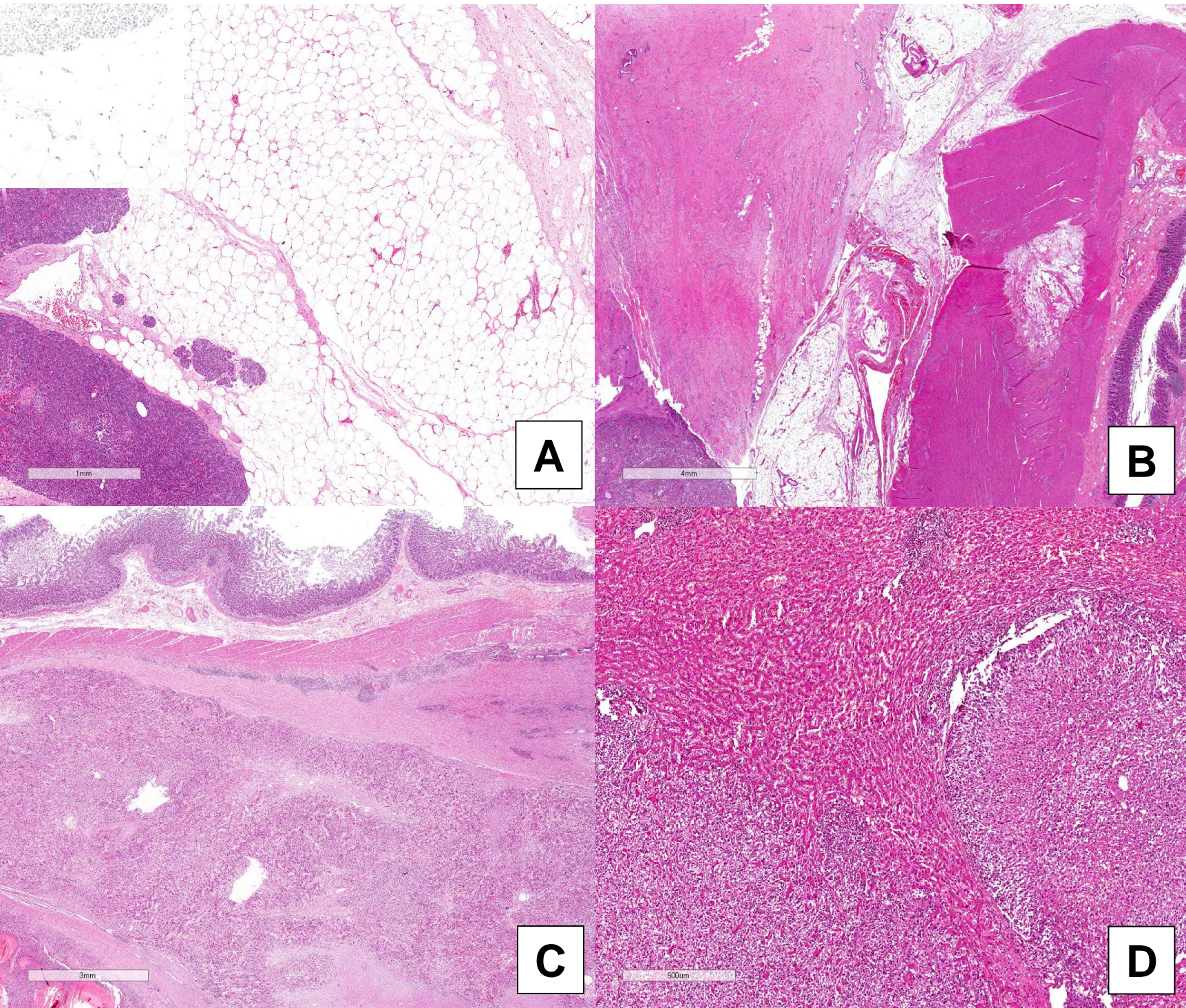


# Prognostic value of microscopic evaluation of organ infiltration and visceral resection margins (VRM) in patients with retroperitoneal sarcomas (RPS).

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## ABSTRACT

**Background.** Surgery with gross margin clearance (R0 and R1) is the standard treatment for RPS and visceral resection has been proposed even in the absence of macroscopic visceral infiltration. Formal definition and margin sampling procedures for pathological evaluation are lacking for RPS. **Aims.** This study investigated visceral resection margins (VRM) as well as viscera infiltration (VI) and their association with patient survival. **Methods.** Primary RPS (2009-2014) VRM were sampled for each resected organ and classified (+/-). Relationship between neoplasm and resected organ were sampled and organ VI classified (+/-). **Results.** 207 Pts, VRM +ve 25(12%), VRM –ve 182 (88%); VI +ve 140 (82%); VI –ve 37 (18%). OS (VRM-ve & VI+ve) VS (VRM-ve & VI-ve) (HR = 3.56; 95%CI 1.15-11.00, P = .028); (VRM+ve) VS (VRM-ve & VI-ve)(HR = 7.76; 95%CI 2.18-27.65, P = .002) after adjustment from known prognostic features. **Conclusions.** After liberal multivisceral resection for primary RPS: 80% of patients have infiltrated organs at some extent. VRM are positive in up to 10%. Visceral resection is justified even in the absence of macroscopic infiltration. Systematic evaluation of microscopic involvement of adjacent viscera may stratify prognosis.



**Visceral Resection Margin and Visceral Infiltration.** A. Positive pancreatic margin, insert (200x) shows positive immunohistochemistry for mdm2. B. Infiltration of perivisceral colon adipose tissue by a dedifferentiated liposarcoma. C. Early infiltration (i.e. contact with muscular tunica) of small intestine by a leiomyosarcoma. D. Dedifferentiated liposarcoma infiltrating hepatic tissue.

## OBJECTIVES

Since neither uniform surgical approach nor pathology sampling procedure and reporting in RPS is determined and universally accepted, this study investigated visceral resection margins (VRM) as well as viscera infiltration (VI) and their association with patient survival in a centre performing multivisceral resection for primary RPS.

## METHODS

Primary RPS (2009-2014) were extracted from a prospectively maintained database. Sampling procedure followed the rule of one block for tumor cm; it also included 1) resection margins of the viscera, and 2) relationship between viscera and neoplasm. VRM were classified as follow: negative, positive with low-grade component, and positive with high-grade component. Also, VI was classified as follow: absence of infiltration, infiltration of perivisceral fat, early infiltration (i.e. renal/adrenal capsule, muscular fascia, contact with muscular tunica of hollow viscera), and infiltration of the viscera. Univariate survival analysis was performed with the Cox proportional hazard model and log-rank test as appropriate. Significant variables at univariate analysis were adjusted in a multivariate Cox regression model.

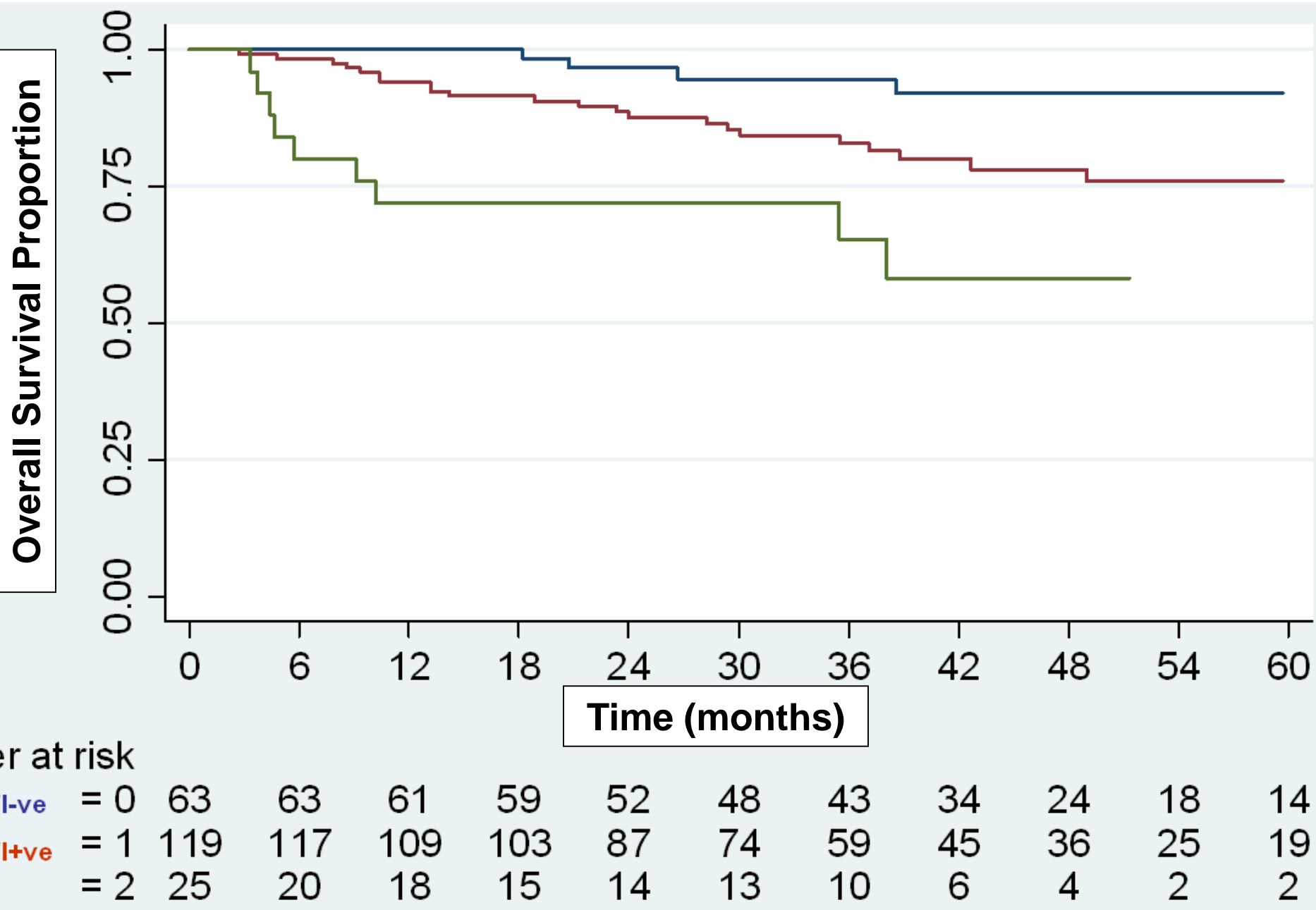
**Patients Characteristics - 207 Pts w/ primary RPS surgically treated**

Gender	Histology	CT	FU from bio (mo)
F/M 86/121	DD-LPS 76	none 153	1st Qu. 23.97
Age	WD-LPS 52	pre 37	mean 38.88
1st Qu. 50	LMS 29	post 12	3rd Qu. 51.50
mean 57.42	SFT 17	pre/post 5	
3rd Qu. 67.5	other 33		
Size (cm)	FNCLCC Grade	RT	Status
1st Qu. 13	Grade 1 75	none 169	NED 137
mean 20.81	Grade 2 71	pre 35	AWD 32
3rd Qu. 28	Grade 3 61	post 3	DOD 46
			D4OR 11

**Legend:** Pts: patients; w/: with; RPS: retroperitoneal sarcoma; F: female; M: male; Qu: quartile; DD: dedifferentiated; LPS: liposarcoma; WD: well differentiated; LMS: leiomyosarcoma; SFT: solitary fibrous tumor; CT: chemotherapy; pre: neoadjuvant; post: adjuvant; RT: radiation therapy; FU: follow-up; bio: biopsy; mo: months; NED: no evidence of disease; AWD: alive with disease; DOD: dead of disease; D4OR: dead for other reasons.

## RESULTS

There were 207 patients, followed for a median of 42 months. Visceral resection margin (VRM) were negative in 182 (88%) patients and positive in 25 (12%); 17 (8%) had at least two positive margins. Moreover positive VRM were with low-grade component, and high-grade component in 15 (7%), and 10 (5%) patients, respectively. Visceral infiltration (VI) was absent, perivisceral, early, and visceral in 37 (18%), 22 (11%), 40 (23%), and 100 (48%) patients respectively.



At multivariable analysis, VRM were not associated with considered clinical-pathologic features. Older patients (OR=1.04; 95%CI 1.01 - 1.07; P=.002) those having larger tumours (OR=1.10; 95%CI 1.05 - 1.16, P<.001), and affected by a liposarcoma (OR=2.85; 95%CI 1.17 - 6.94; P=.021; compared to leiomyosarcoma) were at higher risk of organ infiltration. After adjustment for known prognostic features (patient age, tumor histology, grade, and size), patients having VRM negative and VI positive had a worse overall survival (OS) than patients without organs and VRM infiltration (HR = 3.56; 95%CI 1.15-11.00, P = .028). Patient having positive visceral resection margins had a worse OS than patients without VI and VRM infiltration (HR = 7.76; 95%CI 2.18-27.65, P = .002).

## CONCLUSIONS

- After liberal multivisceral resection for primary RPS: 80% of patients have infiltrated organs at some extent and VRM are positive in up to 10%.
- Age, size and histotype are associated with VI, whereas VRM is an independent prognostic factor.
- VRM impact on OS may reflect either presence of residual disease or particular aggressiveness.
- Adequate visceral resection is justified even in the absence of macroscopic infiltration.
- Systematic evaluation of microscopic involvement of adjacent viscera and their margin status may contribute to prognostic stratification.



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